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Predictive value of circulating tumor DNA in patients with advanced HPV16-positive cervical cancer treated with VB10.16 in combination with atezolizumab

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Background: Use of circulating tumor DNA (ctDNA) has potential value as a minimally invasive approach for the diagnosis, monitoring, and management of cancer patients. Here, we investigated the potential of using HPV16 ctDNA levels as a predictive biomarker of clinical response to the therapeutic HPV16-specific cancer vaccine VB10.16, designed using a unique modular vaccine technology based on linking antigens to a CCL3L1 targeting module and developed to treat HPV16-associated premalignant and malignant lesions, in combination with atezolizumab in patients with advanced cervical cancer.

Methods: Patients with recurrent or metastatic HPV16-positive cervical cancer were enrolled and received up to 11 doses of 3 mg VB10.16 intramuscularly in combination with intravenous atezolizumab 1200 mg for up to 48 weeks or until disease progression or unacceptable toxicity. Anti-tumor activity was evaluated using RECIST 1.1 criteria. Blood samples were collected at baseline and every 9 weeks to quantify HPV16 ctDNA in plasma by digital PCR (dPCR). The study was approved by the national regulatory authorities and Independent Ethic Committees (NCT04405349).

Results: Of the 47 patients included in the efficacy population, the objective response rate was 19% in the overall population and 29% in PD-L1+ patients (cutoff date Dec 22, 2022).
25 of these patients had detectable baseline levels of HPV16 ctDNA and available post-baseline samples. All patients with clinical response also demonstrated molecular response (>50% decrease in HPV16 ctDNA level). Early on-treatment decreases of HPV16 ctDNA levels (week 9-11 post-baseline) were significantly correlated with disease control (11/16 patients with disease control vs 1/9 patients with progressive disease, $p = 0.011$). In contrast, increase in on-treatment levels of HPV16 ctDNA was observed in the majority of patients with progressive disease, indicating that early changes in HPV16 ctDNA levels may predict clinical outcome.

Conclusions:
The data suggest that molecular response and early changes in HPV16 ctDNA are promising predictive biomarkers in patients with HPV16-positive recurrent or metastatic cervical cancer treated with VB10.16 in combination with atezolizumab.

Keywords: Vaccine, clinical study, biomarkers, tumor antigens
(Max 400 words)